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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/879,792	06/13/2001	Yonghong Xiao	02973.00035	3733

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EXAMINER	
RAMIREZ, DELIA M	

ART UNIT	PAPER NUMBER
1652	15

DATE MAILED: 08/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/879,792	XIAO ET AL.	
	Examiner	Art Unit	
	Delia M. Ramirez	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the c rrespondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 June 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15,22-24,69-71 and 74-83* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1-8,11-13,22,23,70 and 71* is/are allowed.

6)☒ Claim(s) *74-83* is/are rejected.

7)☒ Claim(s) *9,10,14,15,24 and 69* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 June 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Application

Claims 1-15, 22-24, 69-71, 74-83 are pending.

Applicant's amendment of claim 69, cancellation of claims 16-21, 25-68, 72-73, and addition of claims 74-83 in Paper No. 14, filed on 6/10/2003 is acknowledged.

Applicant's submission of a declaration in regard to the public availability of a biological deposit, and a declaration under Rule 131 by Inventors Y. Xiao and R. Gedrich is acknowledged.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Drawings

1. The formal drawings submitted on 6/10/2003 have been reviewed and are approved by a draftsperson under 37 CFR 1.84 or 1.152.

Claim Objections

2. Claims 9-10, 14-15, 24 and 69 are objected to because of the following informalities: for clarity, it is suggested that the term "a coding sequence of" be replaced with "the coding sequence of". Appropriate correction is required.

Claim Rejections - 35 USC § 112, Second Paragraph

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 74-83 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5. Claims 74-75 (claims 76-83 dependent thereon) are indefinite in the recitation of "probe selected from the group consisting of: (a) a first polynucleotide.....; and (b) a second polynucleotide.." as it is unclear what the meaning of the terms "first" and "second" is within the context of the claims. As written, it is unclear ff the terms "first" and "second" are recited just to indicate that the group consists of two items. If this is the case, such terms are redundant since the terms "(a)" and "(b)" are already indicating that there are two items in the group. For examination purposes, the terms "first" and "second" will not be given patentable weight when they are first recited. In regard to the recitation of "the first polynucleotide" in part (b), the term "first" will be interpreted as "the polynucleotide of (a)", and the term "second" will be interpreted as "said". Correction is required.

6. Claims 74-83 are indefinite in the recitation of "polynucleotide is at least % identical to the at least 225 contiguous nucleotides" or "polynucleotide and the at least 225 contiguous nucleotides ...are at least % identical" as it is unclear which is the basis for comparison. As written, one cannot determine if the % identity is based on sequence, length, etc. For examination purposes, it will be assumed that the terms recite "polynucleotide is at least % sequence identical to the at least 225 contiguous nucleotides" or "polynucleotide and the at least 225 contiguous nucleotides ...are at least % sequence identical". Correction is required.

7. Claims 74-75 (claims 76-83 dependent thereon) are indefinite in the recitation of "polynucleotide that hybridizes under stringent conditions along the full length of at least 225

contiguous nucleotides of the nucleotide sequence shown in SEQ ID NO: 11 (cDNA insert of plasmid pCRII-TMSP3), wherein the second polynucleotide is at least 70% identical to the at least 225 contiguous nucleotides of the first polynucleotide.." for the following reasons. The claims as written require that the hybridization occurs along the full length of at least 225 contiguous nucleotides of the polynucleotide of SEQ ID NO: 11 (or cDNA insert of plasmid pCRII-TMSP3) and they also require that the polynucleotide claimed be at least 70% sequence identical to at least 225 contiguous nucleotides of the complete complement of SEQ ID NO: 11 (or the complete complement of the cDNA insert of plasmid pCRII-TMSP3). Since hybridization may occur such that not every single nucleotide in the 225 contiguous nucleotide fragment is perfectly matched even at highly stringent conditions, it is unclear as to how one can determine hybridization along the full length of another polynucleotide. Furthermore, as written, it is unclear if the 70% sequence identity limitation refers to the corresponding complement of the 225 contiguous nucleotide fragment which hybridizes as recited or if the identity limitation applies to a different 225 contiguous nucleotide fragment. For examination purposes, the term will be interpreted as "polynucleotide that hybridizes under stringent conditions selected such that the Tm is 12-20 C lower than the Tm calculated by the equation of Bolton and McCarthy, as recited in the claim, to the polynucleotide of SEQ ID NO: 11 (cDNA insert of plasmid pCRII-TMSP3), wherein said polynucleotide is at least 70% sequence identical to any fragment of the complete complement of the polynucleotide of SEQ ID NO: 11 wherein said fragment is at least 225 nucleotides long..". Correction is required.

Claim Rejections - 35 USC § 112, First Paragraph

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 74-83 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

10. Newly added claims 74-83 are directed in part to any polynucleotide which hybridizes to the polynucleotide of SEQ ID NO: 11 or the cDNA insert of plasmid pCRII-TMSP3 under stringent conditions selected such that the Tm of the hybrid is 12-20 C lower than the Tm calculated by the equation of Bolton and McCarthy as recited in the claims, wherein said polynucleotides are at least 70%, 75%, 90%, 96% or 98% sequence identical to any fragment of the complete complement of the polynucleotide of SEQ ID NO: 11 or the cDNA insert of plasmid pCRII-TMSP3, and wherein said fragment is at least 225 nucleotides long. See claim interpretation above. While the Examiner has found support in the specification (page 14, line 22, page 15, line 5) for the stringent hybridization conditions as recited in the claims, the Examiner has been unable to locate adequate support for a polynucleotide which hybridizes under the conditions recited and has at least 70%, 75%, 90%, 96% or 98% sequence identity to any fragment of the complete complement of the polynucleotide of SEQ ID NO: 11 or the cDNA insert of plasmid pCRII-TMSP3. Thus there is no indication that polynucleotides which

hybridize under the stringent conditions recited and have the recited % sequence identity to any fragment of the complete complement of the polynucleotide of SEQ ID NO: 11 or the cDNA insert of plasmid pCRII-TMSP3 were within the scope of the invention as conceived by Applicants at the time the application was filed. Accordingly, Applicants are required to cancel the new matter in the response to this Office Action.

11. Claims 74-83 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

12. This rejection, which has been discussed at length in Paper No. 9, mailed on 9/10/2002 and Paper No. 11, mailed 3/10/2003, has been previously applied to claims 27, 69-71 and is now applied to newly added claims 74-83 for the reasons of record and the reasons set forth below.

13. Applicants argue that the claims now recite specific hybridization conditions and that the recited polynucleotides have the function of being able to detect the recited coding sequences. According to Applicants, whether the recited probes do or do not have another function is irrelevant and need not to be described.

14. Applicant's arguments have been fully considered but are not deemed persuasive to avoid the rejection of newly added claims 74-83. Claims 74-83 are still drawn to a genus of polynucleotides of any function wherein said polynucleotides hybridize to the polynucleotide of SEQ ID NO: 11 or the cDNA insert of plasmid pCRII-TMSP3 under stringent conditions

selected such that the hybrid Tm is 12-20 C lower than the Tm calculated by the equation of Bolton and McCarthy as recited in the claims, wherein said polynucleotides are at least 70%, 75%, 90%, 96% or 98% sequence identical to any fragment of the complete complement of the polynucleotide of SEQ ID NO: 11 or the cDNA insert of plasmid pCRII-TMSP3, and wherein said fragment is at least 225 nucleotides long. See claim interpretation in claim rejections under 35 USC 112 second paragraph.. While the claims recite that the polynucleotides are used in a hybridization assay to detect a polynucleotide encoding the polypeptide of SEQ ID NO: 2, there is no recitation of the specific biological function of these polynucleotides. The genus of polynucleotides claimed is a large variable genus which can potentially encode a large number of proteins of unknown function. Thus, the recitation of "wherein use of the polynucleotide probe in a hybridization assay detects a coding sequence for the amino acid sequence shown in SEQ ID NO: 12" does not indicate the biological function of the claimed polynucleotides. As previously indicated, the specification fails to disclose other functions for the claimed polynucleotides, does not disclose the critical structural elements required in a polynucleotide to display serine protease activity, nor does it disclose which 225 nucleotides are essential for serine protease activity. Furthermore, the state of the art as indicated previously, teaches that structural homologs may not share the same function. Since the specification only discloses a single species of the claimed invention, one cannot reasonably conclude that the claimed invention is adequately described.

15. Claims 1, 4-6, 9-11, 14-15, 22, 24, and 69-71 were rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement in regard to a biological

deposit. In view of Applicant's submission of a statement indicating that the biological deposit was made under the terms of the Budapest Treaty and that it will be made publicly available without restrictions or conditions to the public upon issuance of a patent on the instant application, this rejection is hereby withdrawn.

16. Claims 74-83 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polynucleotide consisting of 225 contiguous nucleotides of the polynucleotide of SEQ ID NO: 11, does not reasonably provide enablement for polynucleotides of any function wherein said polynucleotides hybridize to the polynucleotide of SEQ ID NO: 11 or the cDNA insert of plasmid pCRII-TMSP3 under stringent conditions selected such that the hybrid Tm is 12-20 C lower than the Tm calculated by the equation of Bolton and McCarthy as recited in the claims, wherein said polynucleotide is at least 70%, 75%, 90%, 96% or 98% sequence identical to any fragment of the complete complement of the polynucleotide of SEQ ID NO: 11 or the cDNA insert of plasmid pCRII-TMSP3, and wherein said fragment is at least 225 nucleotides long. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

17. This rejection, which has been discussed at length in Paper No. 9, mailed on 9/10/2002 and Paper No. 11, mailed 3/10/2003, has been previously applied to claims 27, 69-71 and is now applied to newly added claims 74-83 for the reasons of record and the reasons set forth below.

18. Applicants argue that newly added claims 74-83 are directed to polynucleotides that detect a coding sequence and that such use is enabled in the specification. Furthermore,

Applicants argue that the claims do not recite polynucleotides that hybridize under any conditions but rather to specific hybridization conditions. Therefore, it is Applicant's opinion that the specification is enabling for the entire scope of the claims.

19. Applicant's arguments have been fully considered but are not deemed persuasive to avoid the rejection in regard to newly added claims 74-83. As indicated above, the instant claims are still drawn to polynucleotides of any function wherein said polynucleotides hybridize to the polynucleotide of SEQ ID NO: 11 or the cDNA insert of plasmid pCRII-TMSP3 under specific stringent conditions as recited in the claims, wherein said polynucleotides are at least 70%, 75%, 90%, 96% or 98% sequence identical to any fragment of the complete complement of the polynucleotide of SEQ ID NO: 11 or the cDNA insert of plasmid pCRII-TMSP3, and wherein said fragment is at least 225 nucleotides long. While the claims recite that the claimed polynucleotides are used for detecting polynucleotides encoding the polypeptide of SEQ ID NO: 2, such recitation does not provide any indication as to the actual biological function. See discussion above. Furthermore, as previously indicated, the specification does not provide any information as to other biological functions for such polynucleotides, does not describe which 225 contiguous nucleotides of the polynucleotide of SEQ ID NO: 11 are required for serine protease activity, and there is no information as to the critical structural elements required in a polynucleotide to encode a serine protease. While making polynucleotides as claimed may not constitute undue experimentation, determining their use would require undue experimentation since, as indicated in the state of the art, assigning function based solely on structural homology is highly unpredictable. Therefore, in view of the information provided, the lack of relevant examples, and the state of the art in regard to the unpredictability of determining function based

on structural homology, one of skill in the art would have to go through the burden of undue experimentation in order to enable the full scope of the claimed invention.

Claim Rejections - 35 USC § 102

20. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

21. Claims 69-71 were rejected under 35 U.S.C. 102(b) as being anticipated by Hillier et al. (GenBank accession number R78581; cited in the IDS). In view of Applicant's amendment of claims 69-71, which are now directed to the polynucleotide of SEQ ID NO: 11, a polynucleotide encoding the polypeptide of SEQ ID NO: 12 or a polynucleotide comprising the cDNA of plasmid pCRII-TMSP3, this rejection is hereby withdrawn. It is also noted that the polynucleotide of Hillier et al. does not comprise at least 225 contiguous nucleotides of the polynucleotide of SEQ ID NO: 11, therefore it does not anticipate newly added claims 74-83.

22. Claims 69-71 were rejected under 35 U.S.C. 102(b) as being anticipated by Paolini-Giacobino et al. (Genomics 44:309-320, 1997; cited in the IDS). In view of Applicant's amendment of claims 69-71 as indicated above, this rejection is hereby withdrawn. It is also noted that the polynucleotide of Paolini-Giacobino et al. does not comprise at least 225 contiguous nucleotides of the polynucleotide of SEQ ID NO: 11, therefore it does not anticipate newly added claims 74-83.

23. Claims 69-71 were rejected under 35 U.S.C. 102(a) as being anticipated by Kim et al. (Biochim. Biophys. Acta 1518:204-209; March 19, 2001; SPTREMBL accession number Q9BYE2, GenBank accession number AB048796).). In view of Applicant's submission of a

declaration under 37 CFR 1.131 by inventors Y. Xiao and R. Gedrich, stating that the instant invention was conceived and reduced to practice prior to the publication date of the reference by Kim et al., this rejection is hereby withdrawn. While the teachings of Kim et al. would anticipate newly added claims 74-83, in view of Applicant's declaration, this rejection would not apply to newly added claims 74-83.

24. Claims 74-83 are rejected under 35 U.S.C. 102(a) as being anticipated by Dias Neto et al. (GenBank accession number AW845106, May 19, 2000). Dias Neto et al. teaches a polynucleotide which comprises 285 consecutive nucleotides of the polynucleotide of SEQ ID NO: 11. See attached alignment. As such, claims 74-83, which are directed in part to a polynucleotide which comprises at least 225 contiguous nucleotides of the polynucleotide of SEQ ID NO: 11 or the cDNA of plasmid pCRII-TMSP3, are anticipated by the polynucleotide of Dias Neto et al.

Allowable Subject Matter

25. Claims 1-15, 22-24, 69-71 are allowable over the prior art of record.

Conclusion

26. Applicant's amendment, which added claims 74-83, necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

27. Applicants are requested to submit a clean copy of the pending claims (including amendments, if any) in future written communications to aid in the examination of this application.

28. Certain papers related to this application may be submitted to Art Unit 1652 by facsimile transmission. The FAX number is (703) 308-4556. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If Applicant submits a paper by FAX, the original copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (703) 306-0288. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (703) 308-3804. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Delia M. Ramirez, Ph.D.
Patent Examiner
Art Unit 1652

DR
July 29, 2003

REBECCA E. PROUTY
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